

REMARKS

This application has been amended in a manner that is believed to place it in condition for allowance at the time of the next Official Action.

Claims 19-39 are pending in the present application. Support for claims 19-39 may be found in original claims 1-18. Original claims 1-18 have been canceled.

In the outstanding Official Action, claims 13, 17, and 18 were rejected under 35 USC §112, second paragraph, and 35 USC §101 for reciting a "use" of a composition without setting forth any steps involved in the "use" or process. Applicants believe that the present amendment obviates this rejection.

As noted above, claims 13, 17, and 18 have been canceled. New claims 19-39 have been added. In particular, the Examiner's attention is respectfully directed to claims 31 and 35-39. The subject matter of these claims was originally recited in claims 13, 17 and 18 but is not recited in terms of a method as preferred under United States patent practice.

Claims 1-3, 4, 5, 6, 8, 12, and 16-18 were rejected under 35 USC §112, second paragraph, as allegedly being indefinite for particularly pointing out and distinctly claiming the subject matter which applicants regard as the invention. This rejection is respectfully traversed.

In imposing the rejection, the Official Action alleges that the disclaimer or proviso set forth in claim 1 and now

appearing in claim 19, is indefinite. However, applicants believe that the terminology is definite to one skilled in the art.

As the Examiner is aware, so long as the boundaries of the patent protection sought are set forth definitively, albeit with a proviso, the claim complies with the requirements of 35 USC §112, second paragraph. *In re Duva*, 387 F.2d 402, 156 USPQ 90 (CCPA 1967). Moreover, the Examiner's attention is respectfully directed to MPEP Statute 2173.05(i), wherein it is explained that the current view of the courts that there is nothing inherently ambiguous or uncertain about an exclusionary proviso so long as it has basis in the original disclosure. With that in mind, the Examiner's attention is respectfully directed to page 3 of the present specification wherein the proviso is explicitly disclosed.

Thus, in view of the above, applicants believe that the proviso is definite to one skilled in the art.

Claims 1-3, 4, 5, 6, 8, 12, 16 and 18 were also rejected for reciting the terms "all the coupling function", "preferably", "in particular", and/or "more particular". However, as noted above, claims 1-18 have been canceled. In drafting new claims 19-39, applicants believe that these terms are no longer recited in the claims.

Thus, in view of the above, applicants believe that claims 19-39 are definite to one skilled in the art.

In the outstanding Official Action, claims 1-18 were rejected under 35 USC §102(b) as allegedly being anticipated by U.S. Patent 5,021,571, or U.S. Patent 5,334,729. This rejection is respectfully traversed.

Applicants believe that neither publication discloses nor suggests the claimed compounds. U.S. Patent 5,021,571 is directed to cyclohexyl EDTPA monoanhydride. U.S. Patent 5,334,729 is directed to compounds derived from the CDTPA and CTTHA compounds.

The claimed compounds are compounds having at least seven coordination sites with radiometals, i.e., having at least three nitrogen atoms, and at least four COOH or PO(OH)<sub>2</sub> groups. The compounds have more than 6 coordination sites and are able to form stable complexes with radiometals of a large size that can be used in therapeutic or diagnostic methods.

For example, this is discussed beginning on page 27 of the present specification, wherein it is described that compounds AL 247 and AL 245 of the present invention show better complexation properties for <sup>153</sup> Sm than EDTMP. In addition, compound AL 245 shows no loss of <sup>153</sup> Sm at either 24, 48, 72 and 96 h in human serum media.

As a result, applicants believe that the claimed invention stands in contrast to the teaching of the two patents wherein the two publications describe complexes between radiometals of little size such as Co<sup>57</sup> and In<sup>111</sup>, and derivatives

of CDTPA and CTTHA wherein the coupling site R to an antibody is located on a coordination site (e.g., a nitrogen atom). Neither publication addresses the stability of such complexes with radiometals of a large size.

As to the derivatives of CDTPA and CTTHA mentioned above, if the coupling site R is located on a coordination site for complexation with metals, instead of being located on the cyclohexan ring as set forth in the claimed compounds, it is unlikely that such a location of the coupling site R on a coordination site would lead to stable complex with a radiometal due to the steric hindrance. Indeed, CDTPA and CTTHA compounds are excluded from the claimed composition.

The claimed compounds according to the present invention are particularly advantageous because they possess a coupling site located in a place of the molecule, i.e. on the cyclohexan, which does not cause steric hindrance with the radioelement linked to the coordination sites. This result is obtained without eliminating a coordination site.

Thus, it cannot be deduced from the cited publications that the claimed compounds, having at least 7 coordination sites would have better complexation properties for radiometals of a large size than equivalent compounds with fewer coordination sites as disclosed in the cited publications.

Applicants believe that the two publications also fail to disclose or suggest the claimed methods. While the CDTPA and

CTTHA compounds are known, CDTPA and CTTHA compounds are only described as intermediary products for the synthesis of derivatives. Neither publication discloses or suggests the claimed methods.

Thus, in view of the above, applicants believe that U.S. Patent 5,021,571 and U.S. Patent 5,334,729 both fail to anticipate or render obvious the claimed invention.

In view of the present amendment and the foregoing remarks, therefore, applicants believe that the present application is now in condition for allowance at the time of the next Official Action. Allowance and passage to issue on that basis is respectfully requested.

The Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 25-0120 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17.

Respectfully submitted,

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APPENDIX:

The Appendix includes the following item(s):

- a Substitute Specification and a marked-up copy of the originally-filed specification